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TITLE: A Randomized, Controlled Trial of Meditation Compared to Exposure Therapy and Education Control on PTSD in Veterans

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14. ABSTRACT
This study consists of a comparative effectiveness trial of Transcendental Meditation (TM) compared to Prolonged Exposure (PE) and education control (EC) groups in Veterans diagnosed with clinically significant PTSD by way of a validated structured interview methodology over a treatment period of three months. Two hundred and ten veterans will participate in this three-arm trial. Testing will be conducted at 0 and 3 months for PTSD symptoms, psychological distress, depression, quality of life, behavioral factors, and physiological/ biochemical mechanisms using validated interview, self-report, and biological measures. Recruitment began in June of 2013. We hypothesize that TM will be non-inferior to PE on the primary outcome of the study and superior to EC on PTSD study outcomes. This will be a multidisciplinary, collaborative research project comprising investigators from the San Diego VA Healthcare System, the University of California at San Diego and Maharishi University of Management Research Institute. Given a sample of 210 patients, an alpha level of .05 for declaring statistical significance, equal standard deviations, and an attrition rate of 20%, estimated power levels are ≥.90.

15. SUBJECT TERMS
PTSD, transcendental meditation, exposure therapy, clinical trial

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A Randomized, Controlled Trial of Meditation Compared to Exposure Therapy and Education Control on PTSD in Veterans
Partnering PI: Dr. Thomas Rutledge

Year 4 Annual Technical Report, August 2016.

INTRODUCTION:

Posttraumatic stress disorder (PTSD) is a common and disabling condition among Veterans, with few efficacious treatments available. The purpose of this clinical trial is to: 1) To evaluate effects of Transcendental Meditation (TM) vs. Prolonged Exposure (PE) and education control (EC) controls on PTSD; and 2) To evaluate effects of TM vs. PE and EC on PTSD symptoms, depression, anger, quality of life, and physiological/biochemical stress markers. Prior evidence supports TM as a treatment for anxiety and stress symptoms; however, the efficacy of TM as a standalone treatment for psychiatric anxiety disorders is unknown at this time.

BODY:

Task 1: Final DoD ORP approval was given for our staff to begin recruitment on May 31, 2013. This approval came after we made several human subjects-related adjustments based upon DoD ORP requests. The most significant of these requests involved receiving approval from the VASDHS IRB to do consenting over the phone prior to conducting initial phone screens.

Task 2: Hiring and Training of Staff. We completed the hiring of our three full-time staff coordinators and a 50% time Prolonged Exposure study therapist, consistent with the hiring plan proposed in our research proposal.

Task 3: We completed our Case Report Forms and Operations Manuals during this period and did some minor edits. Study statistician, Dr. Rainforth, completed the MS Access database for data entry personnel at VASDHS. Piloting of this database took place. Dr. Rainforth and the data manager oversee the data entry and database management process and consult weekly.

Task 4 thru 9 – We began recruitment, screening of subjects, baseline testing, and randomization of subjects on June 3, 2013. The staff continues using a number of effective angles on recruitment, including the posting of flyers at the VA, giving presentations to community Veterans groups, placing information in VA and Veterans newsletters, and presenting the study to nurses and health-care providers at the VASDHS for referrals. An Internet website for recruitment was also developed and approved by our IRB bodies. We have also purchased advertisement space in local San Diego newspapers that contain sections targeting military populations and potential research participant populations.

As of the beginning of September, 2016 (38 months of recruitment), we have now enrolled and randomized 200 participants to treatment. This number is slightly below our projected recruitment rate of 210 at this stage. On a monthly basis, or randomization has ranged from 2-10 participants per month. All three treatment arms are operational. Of the 200 randomized participants, over 90% of the randomized subjects have gotten into treatment or were scheduled

for their first treatment session. Treatment sessions are held at the VASDHS for all treatment arms and last approximately 60-75 minutes. Sessions are provided by trained instructors in each of the treatment arms: Transcendental Meditation, Prolonged Exposure, and PTSD Health Education, and are supervised by the research team for quality control.

No study-related adverse events have been reported to date. Overall approximately 72% of the treatment sessions have been attended.

The Access database for data entry at VASDHS was developed and completed by study statistician, Maxwell Rainforth, and pilot tested by the VA data manager in Spring, 2013. Data entered and stored is under strict quality control procedures. 100% of the data received thus far has been entered. This meets our milestone established of collected data being entered.

Task 10: Overall Project Management has been progressing smoothly. The PI, Dr Nidich at MUMRI and partnering PI, Dr Rutledge at VASDHS, San Diego have engaged in regular conference calls with study investigators, hired staff, and treatment providers, to discuss start-up phase tasks, recruitment, testing of subjects, randomization, and treatment delivery. These conference calls will continue throughout the trial. Additional communication between PI's and investigators takes place throughout the week as needed.

As illustrated in the enrollment table on the next page, our recruitment now stands at 200 out of a current targeted 210 participants. Although this ratio shows that we are 95% of our recruitment goal at this stage of the study, our recruitment rate has dropped in the past 12 months despite maintaining the same recruitment staff and methods over this past year. This reflects a growing level of competition for eligible participants in our facility and extensive use of the CHOICE program referring San Diego Veterans to civilian mental health services. For example, there are now more than six clinical trials for PTSD taking place in the VA San Diego Healthcare System, including another trial evaluating meditation. These recruitment challenges are not likely to change over remainder of 2016.

We have expanded on our recruitment efforts over the past several months, increasing the percentage of time by our research team dedicated to making recruitment calls and attending service meetings and community presentations targeting Veterans in the San Diego community. This has resulted in maintaining an enrollment rate of 4-5 participants per month rather than the targeted 5-6 participants per month. To meet our overall recruitment goal of 210 participants, we have submitted a written request for a three month no-cost extension. A no-cost extension, if approved, would allow us to recruit through the end of September, and use the October-December period to complete treatments and post-testing.

Task 11: Quarterly and Annual Reports
This document represents the study's fourth Annual report. All previous quarterly and annual reports to the DoD were written, submitted and received in a timely manner.

KEY RESEARCH ACCOMPLISHMENTS:

- Study recruitment began on June 3, 2013 following DOD ORP approval.

- We have completed all study hires, with all treatment therapists institutionally approved at the VA San Diego Healthcare System, and active in treatment delivery.
- As of September 30, 2016, we have randomized 200 participants, a pace slightly below our proposed recruitment timeline of 210 participants in the research plan.
- Drs. Nidich, Rutledge, Mills, Rainforth attended all meetings of the Data Safety and Monitoring Board (DSMB), chaired by the study's medical monitor, Dr. Charles Elder, M.D. Other members of the DSMB include Dr. Kerri Boutelle, psychologist, Dr. Arpi Minassian, psychologist, and Dr. Loki Natarajan, biostatistician. The DSMB last met April 2010 to review the progress of the study.
- A member of our research team attended the 2016 Military Health Research Forum in Florida.

REPORTABLE OUTCOMES:

Due to the study being blinded, there are no reportable outcomes. There were no study publications or conference presentations during this past year. It is expected that there will be several publications and conferences presentations in 2017 and beyond following the completion of data collection.

REFERENCES:

None.

APPENDICES:

None

CONCLUSION:

This report summarized the study progress through Year 4. We are meeting all of our Statement of Work targets for the study. Study recruitment began on June 2013 immediately following DoD ORP human subjects approval. All study staff and treatment therapists have been hired and trained, operation manuals completed, and baseline testing and treatment sessions started. As of the end of September 2015, 200 subjects have been randomized, which meets our target goals for the study. The April 2016 Data Safety and Monitoring Board (DSMB) report is included in this annual report. There have been no "substantive" amendments the study protocol. There were no study-related adverse events to date.

SUPPORTING DATA:

Table 1 Overall Enrollment

Quarterly Report		# Randomized	Cumulative Number	Cumulative Target
From	To			
6/1/2013	9/30/2013	24	24	23
10/1/2013	12/31/2013	17	41	41

1/1/2014	3/31/2014	19	60	58
4/1/2013	6/30/2014	18	78	75
7/1/2014	9/30/2014	17	95	93
10/1/2014	12/31/2014	16	111	110
1/1/2015	3/31/2015	16	127	127
4/1/2015	6/30/2015	14	141	144
7/1/2015	9/30/2015	16	157	162
9/30/2015	12/31/2016	11	168	175
1/1/2016	3/30/2016	13	181	197
4/1/2016	6/30/2016	13	194	210
7/1/2016	8/30/2016	6	200	210